

ABSTRACT

The present invention relates to a method of inhibiting graft-versus-host
5 disease in allogeneic hematopoietic stem cell transplant (HSCT) patients by using
L-leucyl-L-leucine methyl ester (LLME) to eliminate selective cytotoxic T cells in
donor lymphocyte infusions (DLI). LLME has been shown to inhibit GVHD in
animal models by selectively inducing apoptosis in natural killer cells and cytotoxic T
cells. The application of LLME to the human clinical HSCT situation, however, has
10 been hampered by HSC toxicity when unseparated marrow is treated at the
concentrations necessary to purge GVHD-inducing T cells prior to infusion. In the
present invention, this problem is circumvented by the LLME *ex vivo* treatment of
DLI administered following transplantation of T cell-depleted HSC. In this setting,
the effects of LLME on HSC contained within the DLI are irrelevant for clinical
15 outcome. In another embodiment, the risk of toxicity to the stem cell population is
avoided by *ex vivo* LLME treatment of donor lymphocytes after separation of CD34⁺
stem cells and then co-administration of the LLME-treated donor CD34⁺ fraction and
the untreated CD34⁺ stem cells.